and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above,] [(ix)] **(vii)** alkoxyalkyl, [(x)] **(viii)** thioalkoxyalkyl, [(xi)] **(ix)** alkylamino, [(xii)] **(x)** dialkylamino, [(xiii)] **(xi)** phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, [(xiv)] **(xii)** phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, [(xv)] **(xiii)** dialkylaminoalkyl, [(xvi)] **(xiv)** alkoxy and [(xvii)] **(xv)** thioalkoxy;

B' cont'd

A' cont'd

n is 1, 2 or 3;

R_2 is hydrogen or loweralkyl;

R_3 is loweralkyl;

R_4 and R_{4a} are independently selected from phenyl [, thiazolyl and oxazolyl] **and substituted phenyl** wherein the phenyl [, thiazolyl or oxazolyl] ring is [unsubstituted or] substituted with a substituent selected from
(i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy;

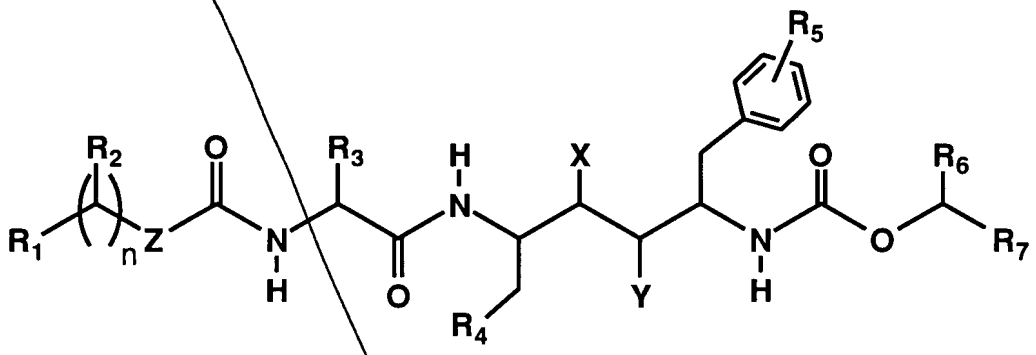
R_6 is hydrogen or loweralkyl;

R_7 is thiazolyl [,] **or** oxazolyl [, isoxazolyl or isothiazolyl] wherein the thiazolyl [,] **or** oxazolyl [, isoxazolyl or isothiazolyl] ring is unsubstituted or substituted with loweralkyl;

X is hydrogen and Y is -OH or X is -OH and Y is hydrogen, with the proviso that X is hydrogen and Y is -OH when Z is -N(R_8)- and R_7 is unsubstituted and with the proviso that X is hydrogen and Y is -OH when R_3 is methyl and R_7 is unsubstituted; and

Z is absent, -O-, -S-, -CH_2- or -N(R_8)- wherein R_8 is loweralkyl, cycloalkyl, -OH or -NHR_{8a} wherein R_{8a} is hydrogen, loweralkyl or an N-protecting group; or a pharmaceutically acceptable salt, ester or prodrug thereof.

2. (amended) A compound of the formula:



wherein R_1 is monosubstituted thiazolyl [,] **or** monosubstituted oxazolyl [, monosubstituted isoxazolyl or monosubstituted isothiazolyl] wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi) cycloalkenylalkyl, [(vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above,] [(ix)] **(vii)** alkoxyalkyl, [(x)] **(viii)** thioalkoxyalkyl, [(xi)] **(ix)** alkylamino, [(xii)] **(x)** dialkylamino, [(xiii)] **(xi)** phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, [(xiv)] **(xii)** phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, [(xv)] **(xiii)** dialkylaminoalkyl, [(xvi)] **(xiv)** alkoxy and [(xvii)] **(xv)** thioalkoxy;

n is 1, 2 or 3;

R_2 is hydrogen or loweralkyl;

R_3 is loweralkyl;

R_4 is phenyl [, thiazolyl or oxazolyl] wherein the phenyl [, thiazolyl or oxazolyl] ring is unsubstituted or substituted with a substituent selected from (i) halo, (ii) loweralkyl, (iii) hydroxy, (iv) alkoxy and (v) thioalkoxy;

R_5 is hydrogen, halo, loweralkyl, hydroxy, alkoxy or thioalkoxy;

R_6 is hydrogen or loweralkyl;

R_7 is thiazolyl [,] **or** oxazolyl [, isoxazolyl or isothiazolyl] wherein the thiazolyl [,] **or** oxazolyl [, isoxazolyl or isothiazolyl] ring is unsubstituted or substituted with loweralkyl;

X is hydrogen and Y is -OH or X is -OH and Y is hydrogen, with the proviso that X is hydrogen and Y is -OH when Z is -N(R_8)- and R_7 is unsubstituted and with the proviso that X is hydrogen and Y is -OH when R_3 is methyl and R_7 is unsubstituted;

B' cont'd

Z is absent, -O-, -S-, -CH_2- or -N(R_8)- wherein R_8 is loweralkyl, cycloalkyl, -OH or -NHR_{8a} wherein R_{8a} is hydrogen, loweralkyl or an N-protecting group; or a pharmaceutically acceptable salt, ester or prodrug thereof.

A' cont'd

3. (amended) The compound of Claim 2 wherein R_1 is monosubstituted thiazolyl or monosubstituted oxazolyl wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi) cycloalkenylalkyl, [(vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above,] [(ix)] **(vii)** alkoxyalkyl, [(x)] **(viii)** thioalkoxyalkyl, [(xi)] **(ix)** alkylamino, [(xii)] **(x)** dialkylamino, [(xiii)] **(xi)** phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, [(xiv)] **(xii)** phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, [(xv)] **(xiii)** dialkylaminoalkyl, [(xvi)] **(xiv)** alkoxy and [(xvii)] **(xv)** thioalkoxy; n is 1; R_2 is hydrogen; R_4 is phenyl or thiazolyl; R_5 is hydrogen; R_6 is hydrogen and R_7 is thiazolyl [,] oxazolyl [, isothiazolyl or isoxazolyl].

4. (amended) The compound of Claim 2 wherein R_1 is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is selected from (i) loweralkyl, (ii) loweralkenyl, (iii) cycloalkyl, (iv) cycloalkylalkyl, (v) cycloalkenyl, (vi) cycloalkenylalkyl, [(vii) heterocyclic wherein the heterocyclic is selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl and wherein the heterocyclic is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, (viii) (heterocyclic)alkyl wherein heterocyclic is defined as above,] [(ix)] **(vii)** alkoxyalkyl, [(x)] **(viii)** thioalkoxyalkyl, [(xi)] **(ix)** alkylamino, [(xii)] **(x)** dialkylamino, [(xiii)] **(xi)** phenyl wherein the phenyl ring is unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy, [(xiv)] **(xii)** phenylalkyl wherein the phenyl ring is unsubstituted or substituted as defined above, [(xv)] **(xiii)** dialkylaminoalkyl, [(xvi)] **(xiv)** alkoxy and [(xvii)] **(xv)** thioalkoxy; n is 1; R_2 is hydrogen; R_4 is phenyl; R_5 is hydrogen; R_6 is hydrogen and R_7 is 5-thiazolyl [,] 5-oxazolyl [, 5-isothiazolyl or 5-isoxazolyl] .

5. (amended) The compound of Claim 2 wherein R_1 is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is loweralkyl; n is 1; R_2 is hydrogen; R_4 is phenyl; R_5 is hydrogen; R_6 is hydrogen; R_7 is 5-thiazolyl [,] 5-oxazolyl [, 5-isothiazolyl or 5-isoxazolyl] ; and Z is -O- or -N(R_8)- wherein R_8 is loweralkyl.

B' cont'd

6. (amended) The compound of Claim 2 wherein R_1 is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is ethyl or isopropyl; n is 1; R_2 is hydrogen; R_3 is methyl or isopropyl; R_4 is phenyl; R_5 is hydrogen; R_6 is hydrogen; R_7 is 5-thiazolyl [,] 5-oxazolyl [, 5-isothiazolyl or 5-isoxazolyl] ; and Z is -O-.

A' cont'd

7. The compound of Claim 2 wherein R_1 is 2-monosubstituted-4-thiazolyl or 2-monosubstituted-4-oxazolyl wherein the substituent is ethyl or isopropyl; n is 1; R_2 is hydrogen; R_3 is isopropyl; R_4 is phenyl; R_5 is hydrogen; R_6 is hydrogen; R_7 is 5-thiazolyl [,] 5-oxazolyl [, 5-isothiazolyl or 5-isoxazolyl] ; Z is -N(R_8)- wherein R_8 is methyl; X is hydrogen and Y is -OH.

B' cont'd

10. (amended) A compound selected from the group consisting of:

A2

(2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-amino)carbonyl)alaninyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

(2S,3S,5S)-5-(N-(N-((2-Isopropyl-4-thiazolyl)methoxycarbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

(2S,3S,5S)-2-(N-(N-((2-Isopropyl-4-thiazolyl)methoxycarbonyl)valinyl)amino)-5-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

(2S,3S,5S)-5-(N-(N-((2-Isopropyl-4-thiazolyl)methoxycarbonyl)alaninyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

(2S,3S,5S)-5-(N-(N-((2-(N,N-Dimethylamino)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

(2S,3S,5S)-2-(N-(N-((2-(N,N-Dimethylamino)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-5-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

[(2S,3S,5S)-5-(N-(N-((2-(4-Morpholinyl)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

(2S,3S,5S)-2-(N-(N-((2-(4-Morpholinyl)-4-thiazolyl)-methoxycarbonyl)valinyl)-amino)-5-(N-((5-thiazolyl)-methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

(2S,3S,5S)-5-(N-(N-((2-(1-Pyrrolidinyl)-4-thiazolyl)methoxycarbonyl)-valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;]

(2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-oxazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-oxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane; **and**

(2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-oxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;

[(2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-isoxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane; and (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-oxazolyl)methyl)amino)-carbonyl)valinyl)amino)-2-(N-((5-isoxazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane;]or a pharmaceutically acceptable salt, ester or prodrug thereof.

Please add the following new claim:

- - 29. (2S,3S,5S)-5-(N-(N-((N-Methyl-N-((2-isopropyl-4-thiazolyl)methyl)-amino)carbonyl)valinyl)amino)-2-(N-((5-thiazolyl)methoxycarbonyl)amino)-1,6-diphenyl-3-hydroxyhexane. - -

REMARKS

This is a response to the Office Action dated July 21, 1994. In the Office Action, the Examiner has (1) requested affirmation of the election of invention, (2) rejected Claims 1-7, 10 and 12-20 as being drawn to an improper Markush group, (3) objected to the specification and rejected Claims 1-7 and 12-20 under 35 U.S.C. 112 , (4) provisionally rejected Claims 1-10 and 12-20 under 35 U.S.C. 101, (5) provisionally rejected Claims 1-10 and 12-20 under 35 U.S.C. 102 and (6) acknowledged that the inventorship has been amended to include Arthur J. Cooper as a joint-inventor. In this response, Applicants request reconsideration of the rejections.

ELECTION OF INVENTION

Applicants affirm the election of the Examiner's restriction group I (i.e., Claims 1-10 and 12-20) as applied to the elected species (i.e., the compound of Claim 8) and related compounds of the invention. The non-elected subject matter of the claims has been cancelled by amendment herein. Applicants reserve the right to file a divisional application claiming the cancelled subject matter.

AMENDMENT

New Claim 29 has been added by amendment herein. Applicants assert that this claim does not introduce new matter, as it claims the compound prepared in Example 1U (page 41).

IMPROPER MARKUSH REJECTION

The Examiner has rejected Claims 1-7, 10 and 12-20 as being drawn to an improper Markush group. The non-elected subject matter of the claims has been cancelled by amendment herein. Applicants reserve the right to file a divisional application claiming the cancelled subject matter. Therefore, the Examiner is respectfully requested to reconsider and withdraw the improper Markush claim rejection.